Hypertension
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Introduction

- **Hypertension is one of the leading causes of the global burden of disease.**

- **Approximately 7.6 million deaths (13–15% of the total) and 92 million disability-adjusted life years worldwide were attributable to high BP in 2001.**

- **Hypertension doubles the risk of CVD:**
- **coronary heart disease (CHD),**
- **congestive heart failure (CHF),**
- **ischemic and hemorrhagic stroke,**
- **renal failure,**
- **and peripheral arterial disease.**
- **large segments of the hypertensive population are either untreated or inadequately treated.**

Epidemiology

- **In the United States approximately 30% (age-adjusted prevalence) of adults, or at least 65 million individuals, have HTN.**

(defined as any one of the following:
-systolic blood pressure 140 mmHg,
-diastolic blood pressure 90 mmHg,
-taking antihypertensive medications).

- **The likelihood of hypertension increases with age, and among individuals age 60, the prevalence is 65.4%.**
- **Obesity and weight gain are strong, independent risk factors for HTN.**
- **It has been estimated that 60% of hypertensives are >20% overweight.**

- **HTN prevalence is related to dietary NaCl intake, and the age-related increase in BP may be augmented by a high NaCl intake.**
- **Low dietary intakes of calcium and potassium also may contribute to the risk of HTN.**
- **The urine sodium-to-potassium ratio is a stronger correlate of BP than is either sodium or potassium alone.**
- **Alcohol consumption, psychosocial stress, and low levels of physical activity also may contribute to HTN.**

- **Blood pressure heritabilities are in the range 15–35%.**
- **In twin studies, heritability estimates of BP are ~60% for males and 30–40% for females.**
- **High BP before age 55 occurs 3.8 times more frequently among persons with a positive family history of hypertension.**

Genetic Considerations

- **Although specific genetic variants have been identified in rare Mendelian forms of hypertension, these variants are not applicable to the vast majority (>98%) of patients with essential hypertension.**

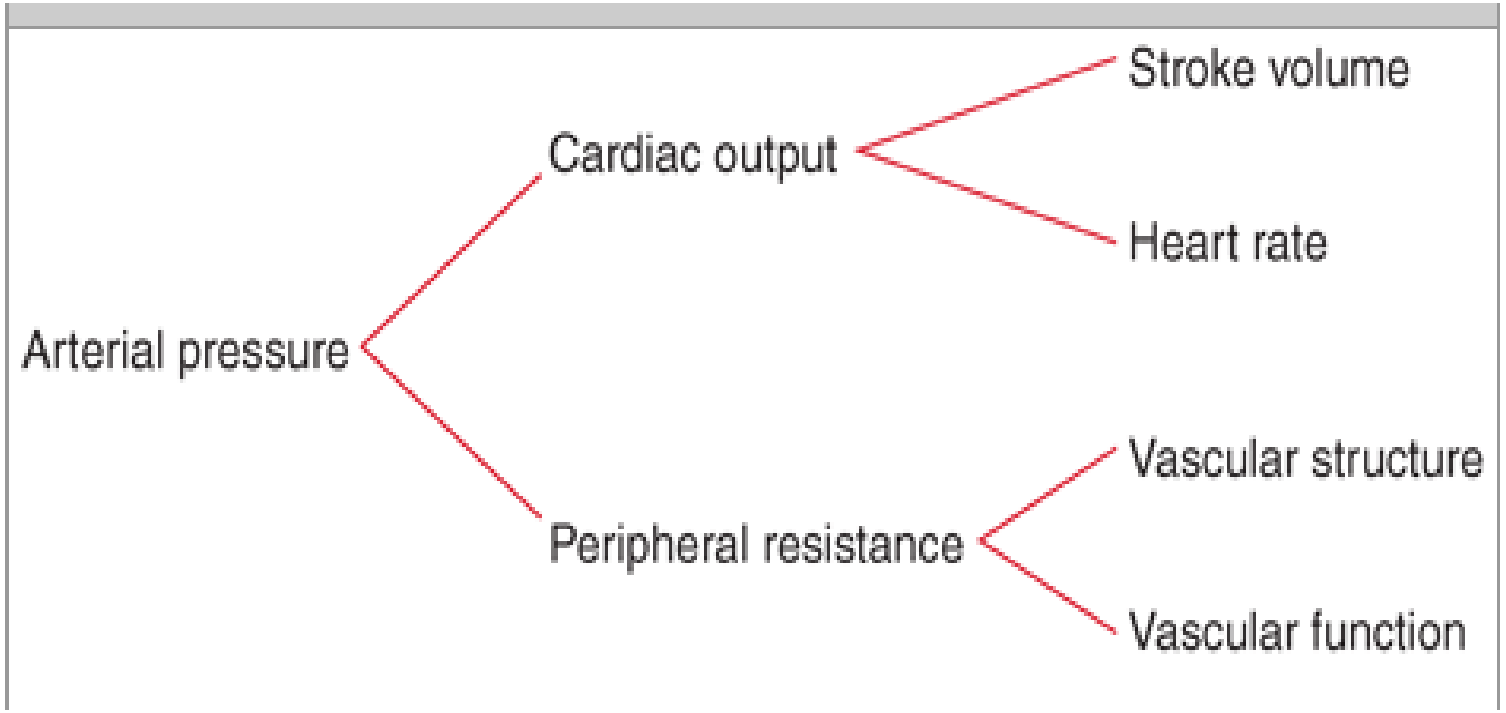
- **For most individuals, it is likely that hypertension represents a polygenic disorder in which a combination of genes acts in concert with environmental exposures to make only a modest contribution to BP.**

- **Further, different subsets of genes may lead to different phenotypes associated with HTN, e.g., obesity, dyslipidemia, insulin resistance.**

- **There may also be genetic determinants of target organ damage attributed to HTN.**
- **Family studies indicate significant heritability of LV mass, and there is considerable individual variation in the responses of the heart to HTN.**
- **Family studies and variations in candidate genes associated with renal damage suggest that genetic factors also may contribute to hypertensive nephropathy.**
- **Specific genetic variants have been linked to CHD and stroke.**

Mechanisms of Hypertension

Cardiac output and peripheral resistance are the two determinants of arterial pressure.



Intravascular Volume

- **Sodium is predominantly an extracellular ion and is a primary determinant of the extracellular fluid volume.**
- **When NaCl intake exceeds the capacity of the kidney to excrete sodium, vascular volume initially expands and cardiac output increases.**

- **As arterial pressure increases in response to a high NaCl intake, urinary sodium excretion increases and sodium balance is maintained at the expense of an increase in arterial pressure.**
- **ESRD is an extreme example of volume-dependent hypertension.**

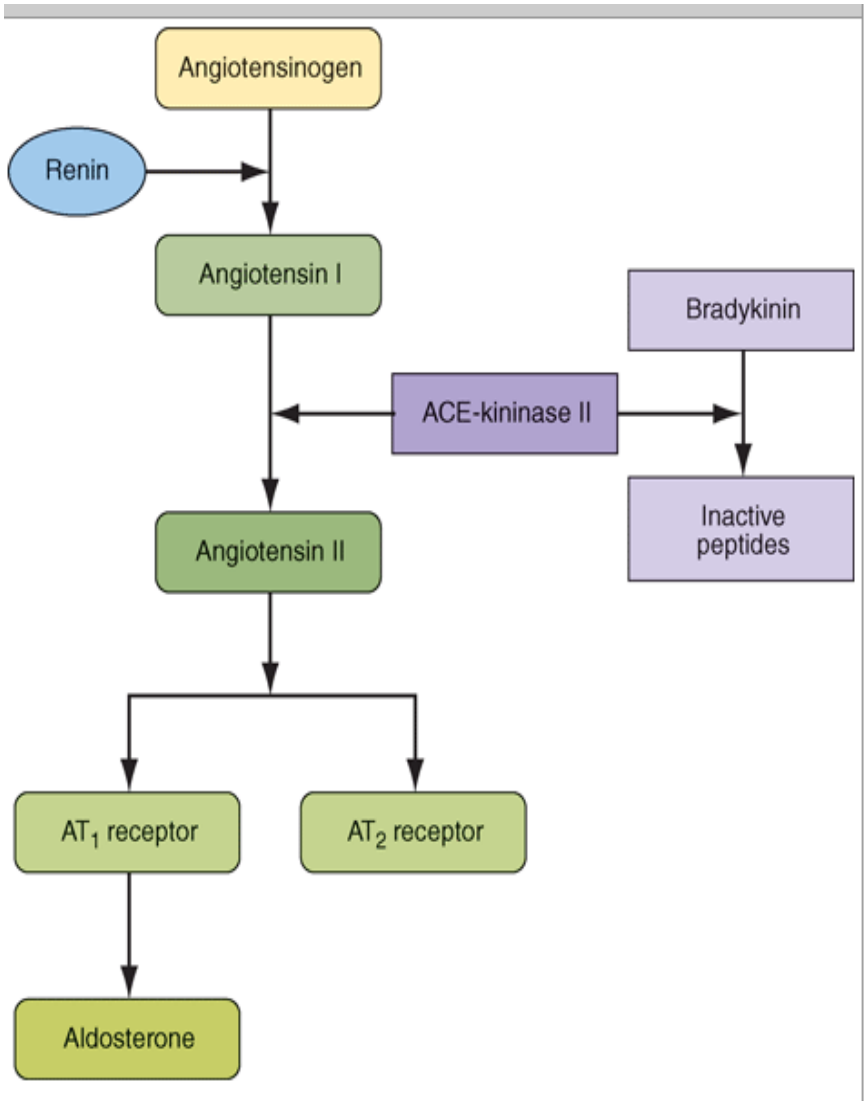
Autonomic Nervous System

- **The three endogenous catecholamines are norepinephrine, epinephrine, and dopamine.**
- **All three play important roles in tonic and phasic cardiovascular regulation.**
- **Norepinephrine and epinephrine are agonists for all adrenergic receptor subtypes, although with varying affinities.**
- **Based on their physiology and pharmacology, adrenergic receptors have been divided into two principal types: α & β.**

- **In both normal-weight and obese individuals, hypertension often is associated with increased sympathetic outflow.**

- **Pheochromocytoma is the most blatant example of HTN related to increased catecholamine production,**

Renin-Angiotensin-Aldosterone Axis



Vascular Mechanisms

- **In hypertensive patients, structural, mechanical, or functional changes may reduce the lumen diameter of small arteries and arterioles.**
- **They have stiffer arteries, and arteriosclerotic patients may have particularly high systolic BP and wide pulse pressures as a consequence of decreased vascular compliance due to structural changes in the vascular wall.**

Pathologic Consequences of Hypertension

- **HTN is an independent predisposing factor for HF, CAD, stroke, renal disease, & peripheral arterial disease.**
- **Heart**
- **Brain**
- **Kidney**
- **Peripheral Arteries**

Defining Hypertension

Table 247-1. Blood Pressure Classification		
Blood Pressure Classification	**Systolic, mmHg**	**Diastolic, mmHg**
Normal	<120	*and* <80
Prehypertension	120–139	*or* 80–89
Stage 1 hypertension	140–159	*or* 90–99
Stage 2 hypertension	≥160	*or* ≥100
Isolated systolic hypertension	≥140	*and* <90

Clinical Disorders of Hypertension

Table 247-2. Systolic Hypertension with Wide Pulse Pressure
1. Decreased vascular compliance (arteriosclerosis)
2. Increased cardiac output.
a. Aortic regurgitation
b. Thyrotoxicosis.
c. Hyperkinetic heart syndrome.
d. Fever.
e. Arteriovenous fistula
f. Patent ductus arteriosus

Table 247-3. Secondary Causes of Systolic and Diastolic Hypertension	
Renal	Parenchymal diseases, renal cysts (including polycystic kidney disease), renal tumors (including renin-secreting tumors), obstructive uropathy
Renovascular	Arteriosclerotic, fibromuscular dysplasia
Adrenal	Primary aldosteronism, Cushing's syndrome, 17α-hydroxylase deficiency, 11β-hydroxylase deficiency, 11-hydroxysteroid dehydrogenase deficiency (licorice), pheochromocytoma
Aortic coarctation	
Obstructive sleep apnea	
Preeclampsia/eclampsia	
Neurogenic	Psychogenic, diencephalic syndrome, familial dysautonomia, polyneuritis (acute porphyria, lead poisoning), acute increased intracranial pressure, acute spinal cord section
Miscellaneous endocrine	Hypothyroidism, hyperthyroidism, hypercalcemia, acromegaly
Medications	High-dose estrogens, adrenal steroids, decongestants, appetite suppressants, cyclosporine, tricyclic antidepressants, monamine oxidase inhibitors, erythropoietin, nonsteroidal anti-inflammatory agents, cocaine
Mendelian forms of hypertension	See Table 247-4

- **Depending on methods of patient ascertainment, ~80–95% of patients are diagnosed as having "essential" HTN (also referred to as primary or idiopathic hypertension).**
- **In the remaining 5–20% of patients, a specific underlying disorder causing the elevation of BP can be identified.**

Rare Mendelian Forms of Hypertension

Disease
Glucocorticoid-remediable hyperaldosteronism
17α-hydroxylase deficiency
11β-hydroxylase deficiency
11β-hydroxysteroid dehydrogenase deficiency (apparent mineralocorticoid excess syndrome)
Liddle's syndrome
Pseudohypoaldosteronism type II (Gordon's syndrome)
Hypertension exacerbated in pregnancy
Polycystic kidney disease
Pheochromocytoma

Approach to the Patient: Hypertension

Table 247-5. Patient's Relevant History
Duration of hypertension
Previous therapies: responses and side effects
Family history of hypertension and cardiovascular disease
Dietary and psychosocial history
Other risk factors: weight change, dyslipidemia, smoking, diabetes, physical inactivity
Evidence of secondary hypertension: history of renal disease; change in appearance; muscle weakness; spells of sweating, palpitations, tremor; erratic sleep, snoring, daytime somnolence; symptoms of hypo- or hyperthyroidism; use of agents that may increase blood pressure
Evidence of target organ damage: history of TIA, stroke, transient blindness; angina, myocardial infarction, congestive heart failure; sexual function Other comorbidities

- **Measurement of Blood Pressure**
- **Physical exam.**
- **Laboratory Testing**

Laboratory Testing

Table 247-6. Basic Laboratory Tests for Initial Evaluation	
System	**Test**
Renal	Microscopic urinalysis, albumin excretion, serum BUN and/or creatinine
Endocrine	Serum sodium, potassium, calcium, ?TSH
Metabolic	Fasting blood glucose, total cholesterol, HDL and LDL (often computed) cholesterol, triglycerides
Other	Hematocrit, electrocardiogram

Treatment Hypertension Lifestyle Interventions

Table 247-7. Lifestyle Modifications to Manage Hypertension	
Weight reduction	Attain and maintain BMI <25 kg/m^2
Dietary salt reduction	<6 g NaCl/d
Adapt DASH-type dietary plan	Diet rich in fruits, vegetables, and low-fat dairy products with reduced content of saturated and total fat
Moderation of alcohol consumption	For those who drink alcohol, consume ≤2 drinks/day in men and ≤1 drink/day in women
Physical activity	Regular aerobic activity, e.g., brisk walking for 30 min/d

Pharmacologic Therapy

- Diuretics
- Blockers of the Renin-Angiotensin System
- Aldosterone Antagonists
- Beta Blockers
- Alpha-Adrenergic Blockers
- Sympatholytic Agents
- Calcium Channel Blockers
- Direct Vasodilators

Hypertensive Emergencies

Table 247–9. Preferred Parenteral Drugs for Selected Hypertensive Emergencies	
Hypertensive encephalopathy	Nitroprusside, nicardipine, labetalol
Malignanthypertension (when IV therapy is indicated)	Labetalol, nicardipine, nitroprusside, enalaprilat
Stroke	Nicardipine, labetalol, nitroprusside
Myocardial infarction/unstable angina	Nitroglycerin, nicardipine, labetalol, esmolol
Acute left ventricular failure	Nitroglycerin, enalaprilat, loop diuretics
Aortic dissection	Nitroprusside, esmolol, labetalol
Adrenergic crisis	Phentolamine, nitroprusside
Postoperative hypertension	Nitroglycerin, nitroprusside, labetalol, nicardipine
Preeclampsia/eclampsia of pregnancy	Hydralazine, labetalol, nicardipine